DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Peggy J. Berry, MBA
VP, Regulatory Affairs and Quality
Amarin Pharmaceuticals Ireland LTD
1430 Route 206, Suite 200
Bedminster NJ, 07921

RE: NDA #202057
VASCEPA® (icosapent ethyl) Capsules, for oral use
MA #63

Dear Ms. Berry:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a "Rapid Overview Webcast Series- Print Invitation" (130285) (print invitation) for VASCEPA® (icosapent ethyl) Capsules, for oral use (Vascepa) submitted by Amarin Pharmaceuticals Ireland LTD (Amarin) under cover of Form FDA 2253. This print invitation is false or misleading because it presents efficacy claims for Vascepa but fails to communicate any risk information associated with its use. Thus, the print invitation misbrands Vascepa within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and makes its distribution violative of the FD&C Act. 21 U.S.C.352(a) & 321(n). *Cf.* 21 CFR 202.1(e)(5).

Background

Below are the indication and summary of the most serious and most common risks associated with the use of Vascepa.[1] According to the INDICATIONS AND USAGE section of the FDA-approved product labeling (PI) (emphasis original):

> VASCEPA® (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia.
> **Usage Considerations:** Patients should be placed on an appropriate lipid-lowering diet and exercise regimen before receiving VASCEPA and should continue this diet and exercise regimen with VASCEPA.
>
> Attempts should be made to control any medical problems such as diabetes mellitus, hypothyroidism, and alcohol intake that may contribute to lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed, if possible, prior to consideration of TG-lowering drug therapy.

[1] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

Limitations of Use:
•The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.
•The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

Vascepa is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to Vascepa or any of its components. The PI also includes Warnings and Precautions regarding laboratory monitoring in patients with hepatic impairment and fish allergy. The most common adverse reaction associated with Vascepa is arthralgia.

Omission of Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials.

The print invitation includes the following claims (emphasis original):

- "**VASCEPA® (icosapent ethyl)**

  Join us to learn more about lowering triglyceride (TG) levels in adult patients with very high TG, including a review of key clinical data for VASCEPA . . . ."

- "**Indication and Limitations of Use**

  VASCEPA is indicated as an adjunct to diet to reduce TG levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

  - The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.
  - The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined."

The print invitation is misleading because it presents efficacy claims for Vascepa but fails to communicate **any** of the risks associated with its use. By omitting the most serious and frequently occurring risks associated with the drug, the print invitation misleadingly suggests that Vascepa is safer than has been demonstrated. We note that the print invitation includes the statement, "*Please see the accompanying full Prescribing Information for VASCEPA*" (emphasis original). However, this statement does not mitigate the misleading omission of risk information from the print invitation.

Conclusion and Requested Action

For the reasons discussed above, the print invitation misbrands Vascepa within the meaning of the FD&C Act, and makes its distribution violative. 21 U.S.C. 352(a) & 321(n). *Cf.* 21 CFR 202.1(e)(5).

OPDP requests that Amarin immediately cease violating the FD&C Act as discussed above. Please submit a written response to this letter on or before December 31, 2013, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Vascepa that contain presentations such as those described above, and explaining your plan for discontinuing use of such materials.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266** or by facsimile at (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA #63 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Untitled Letter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Vascepa comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Ankur Kalola, Pharm.D.
Regulatory Review Officer
Office of Prescription Drug Promotion

{See appended electronic signature page}

Adora Ndu, Pharm.D.
LCDR, USPHS
Acting Team Leader
Office of Prescription Drug Promotion

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ANKUR S KALOLA
12/16/2013

ADORA NDU
12/16/2013